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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,152	01/04/2007	Joacim Elmen	22460-0041001 / 1019US	1052

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
09/16/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/550,152	ELMEN ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *67-97 and 102* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *67-97 and 102* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Claim Rejections - 35 USC § 103

Claims 67-97 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Crooke (US 6,107,094, of record) and Orum et al. (US 2002/0068709, of record).

Crooke teaches at column 12 oligomeric compounds that bind to a target RNA strand and are substrates for dsRNase enzymes. The oligomeric compounds include oligoribonucleotides and other oligomeric compounds having a linear sequence of linked ribonucleoside subunits incorporated therein. The oligoribonucleotides are assembled from a plurality of nucleoside subunits. In certain preferred embodiments at least one of the nucleoside subunits bears a substituent group that increases the binding affinity of the oligoribonucleotide for a complementary strand of nucleic acid. In certain embodiments of the invention, specific nucleoside subunits or internucleoside linkages are functionalized or selected to increase the nuclease resistance of the oligoribonucleotide or oligoribonucleoside. At column 14 Crooke teaches that the oligomeric compounds of the invention are preferably 15-25 nucleotides in length. One embodiment of oligomeric compounds specifically taught by Crooke in examples 24 and 27a are artificial substrates for dsRNAse enzymes. These substrates comprise sense

and antisense strands wherein one or both strands are chemically modified. Crooke exemplifies embodiments where the artificial substrate is 17 and 20 nucleotides in length. Crooke does not teach LNAs as a modified nucleoside subunit.

Orum et al. teach that to be useful an oligonucleotide must have properties such as good resistance to extra- and intracellular nucleases as well as high affinity and specificity for the target. Orum et al. further teach that DNA compounds referred to as Locked Nucleic Acids, which have bicyclic sugars, provide extremely stable duplexes with a target nucleic acid.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the artificial nuclease substrates of Crooke with one or more LNA monomers as taught by Orum et al. Based on the disclosure explicit teachings of Crooke of artificial substrates that contain modified nucleotides and his teaching that modifications are intended to increase nuclease resistance and/or binding affinity of the oligoribonucleotide for a complementary strand of nucleic acid the person of ordinary skill in the art would have reason to make modified substrates and based on the teachings of Orum et al. that inclusion of LNA monomers provide nuclease resistance and extremely stable duplexes the person of ordinary skill would be motivated to make the modified substrate with one or more LNA monomers. Based on the broad disclosure of Crooke that modified nucleotides can be at any position one of ordinary skill would recognize the inclusion of multiple LNA moieties and the placement of these moieties to be a matter of design choice.

Response to Arguments

Applicants argue the double-stranded molecules of Crooke were used only as artificial substrates to test single-stranded oligonucleotides containing 2'-methoxy nucleotides and phosphorothioate internucleotide linkages. Applicants further argue there would be no reason to put LNA into the artificial substrates since Crooke was only using them to explore the mechanism of cleavage by single-stranded oligonucleotides that contained 2'-methoxy nucleotides and the introduction of LNA into the substrates would not serve this purpose. Applicants further argue both Crooke and Orum concern single-stranded antisense compounds designed to elicit dsRNase activity when hybridized to a target mRNA and one would not turn to single-stranded anti-sense molecules to design double-stranded siRNA.

These arguments are not persuasive because there is no teaching in Crooke that the goal of the experiments is testing of 2'-methoxy nucleotides or that assays for dsRNAses are limited to artificial substrates having methoxy substituents. Further, the two examples of Crooke cited in the rejection are double stranded RNAs that have a sense and antisense strand and meet the length requirements of the claims; clearly this reference is not limited to single stranded antisense compounds. Any teaching within Crooke of the desirability and advantages of modified nucleotides applies to these substrates as well as to single-stranded compounds, therefore the teachings of Orum that LNA provides better nuclease resistance and binding affinity is in line with the reasons Crooke sets forth for use of modified nucleotides and provide reason to include LNA in an artificial nuclease substrate.

Applicants argue the rejections does not identify the rationale for the "design choice" that would make the claimed double-stranded compounds obvious and argue Crooke's disclosure is directed to the design of single-stranded oligonucleotides that elicit dsRNase activity against a complementary mRNA and cannot be seen as providing any teaching directed to design choices for double-stranded oligonucleotides much less double-stranded oligonucleotides useful for eliciting siRNA mediated mRNA cleavage.

This argument is not persuasive because, as noted above, Crooke's teachings are not limited to single stranded oligonucleotides; therefore, any disclosure of modified nucleotides is applicable to the double stranded oligonucleotides used in the examples. Such disclosures include the teachings at column 12 that the compounds contemplated by Crooke include both ribonucleotides and deoxynucleotides as well as the teachings at columns 4-6 of specific types of modifications and modification patterns like the "gapmer" motif and the exemplified embodiments of the cited examples which use gapmers. Based on these teachings the person of ordinary skill in the art would recognize the desirability of producing oligonucleotides with several modifications at one or both termini of the two strands. Additionally, because Crooke discloses modified nucleotides generally at columns 4-6 without a requirement that they be placed at particular locations or avoided at particular locations, the person of ordinary skill would recognize that modified nucleotides could be present at any position. Additionally, while applicants attempt to distinguish the claimed compounds as "useful for eliciting siRNA mediated mRNA cleavage", the examiner notes the compounds of Crooke satisfy the

length requirements of the claims and have a sense and antisense strand. They are therefore assumed in the absence of evidence to the contrary to also be useful for this purpose

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is (571)272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita, can be reached on 571-272-2876. The central FAX Number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tracy Vivlemore
Primary Examiner
Art Unit 1635

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